

**REMARKS**Status of the Claims

Claims 1, 2, 5 and 6 are rejected under 35 U.S.C. 112, first paragraph. All other rejections to the claims have been overcome (November 28, 2005, Advisory Action).

Interview Summary

Applicants called the Examiner on December 22<sup>nd</sup> to request clarification as to the remaining enablement rejection of the claims, as in the Advisory Action (November 28, 2005) both compound (claims 1, 2, 5, and 6) and method-of-use (claims 8-12) claims were listed as rejected. The Examiner confirmed that the enablement rejection did apply to the compound claims as the method claims 8-12 had been canceled. Approaches to this rejection were discussed, but no agreement was reached.

Rejection of Specification (New Matter)

In his advisory action dated November 28, 2005, the Examiner maintains that the addition of the label "IC50" to page 48 of the specification constitutes new matter. In response, Applicants have canceled the "IC50" label, but assert that one of skill in the art would recognize the activity range listed therein as IC50 and/or KI values, and almost certainly as IC50 values because of the nature of the assay (discussed in previous two amendments). Applicants respectfully request withdrawal of the new matter rejection.

Rejection of Claims under 35 U.S.C. 112, first paragraph

Claims 1, 2, 5 and 6 remain rejected under 35 U.S.C. 112, first paragraph as no utility for CCR4 antagonists has yet been established. Applicants respectfully traverse. In most references that have been considered by the Examiner the chemokine receptor CCR4 has been of interest, or at least the subject of investigation/consideration, with regard to its potential as a therapeutic target with regard to inflammatory, infectious, and immunoregulatory disorders, particularly inflammatory disorders. *See e.g.* Lloyd et al, *Current Opin. In Pharmacol* 3: pp 443-448 (2003); and Ruth et al., *Arthritis Rheum*, 44(5): pp. 2750-2760 (2001) (both in IDS, November 1, 2005).

Moreover, one of skill in the art would recognize that selective CCR4 inhibitors would be useful in the investigation of CCR4 activity in immunological response models. For example, as CCR4 is known to partner with ligands such as TARC and MDC. *See also e.g.* Lukacs, N. W. *Nat. Rev. Immunol.* 1 pp 108 (2001) (submitted in IDS, November 21, 2003). Anti-TARC and anti-MDC antibodies are reported to have efficacy in murine asthma models and other *in vivo* studies

have confirmed the use of such antibodies in preventing immunological responses. *See e.g.* Kawasaki, S. et al., *J. Immunol*, 166, pp 2055 (2001); and Wakugawa, M et al., *Drugs News Perspect.* 15(3) pp 175 (2002) (submitted in IDS, November 1, 2005). Accordingly, one of skill in the art would find selective inhibitors of CCR4, such as those provided by the present invention, useful (at least) in probing the role of CCR4 in the foregoing models. Thus, given the information in the specification coupled with what is known in the art, one of skill would be able to make and use the compounds of the present invention. Withdrawal of the enablement rejection of the claims is requested.

#### Summary


Applicants believe the present claims and specification are in condition for allowance. The Examiner is invited to contact the undersigned by telephone, at the number listed below, if it is believed that a telephonic communication would facilitate the prosecution of this application.

#### Fees

No additional fees should be due, aside from the fee due for the two-month extension of time. However, if it is determined that an additional fee is due, please charge same to Deposit Account No. 19-3880 in the name of Bristol-Myers Squibb Company.

Respectfully submitted,

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